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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,102	05/01/2001	Dennis A. Carson	220002062900	5759

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EXAMINER

YU, MISOOK

ART UNIT PAPER NUMBER

1642

DATE MAILED: 03/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/847,102

Applicant(s)

CARSON ET AL.

Examiner

MISOOK YU, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 16, 28 and 29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 16, 28, and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 14 December 2005 has been entered.

Claims 1-8, 16, 28, and 29 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new ground of rejection.

Claim Rejections - 35 USC § 112

Claims 1-8, 16, 28, and 29 **remain rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn because applicant's argument is persuasive. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

This new matter rejection is made because of the limitation added in the amendment filed on 06/04/2005, i.e. "the antibody inhibits growth of the malignant cell that expresses the frizzled 5 receptor" in claims 1, and 16, the limitation "wherein the

antibody is effective for immunotherapy of a malignant cell that overexpresses the frizzled 5 receptor" in claim 28.

Applicant argues that according to MPEP 2163 B, there is no *in haec verba* requirement for newly added claim limitations and those limitations can be supported by express, implicit, or inherent disclosure. The specification at original claims 1 and 10, page 22 lines 3-6, Table 2 at page 11, Fig. 8 has the support for the amended claims.

These arguments have been fully considered but found unpersuasive because the instantly claimed antibodies are subgenus of the genus of antibodies contemplated in the specification as originally filed at original claims 1 and 10, page 22 lines 3-6, Table 2 at page 11, Fig. 8. A subgenus is not necessarily described by a genus encompassing it even if a disclosed species upon which it reads according to MPEP 2163 B. As stated in the previous Office action, the application contemplates antibodies that bind to extracellular epitopes of frizzled proteins (total 10 disclosed at Fig. 8). Frizzled 5 is a member of the frizzled protein family. At page 28, lines 9-12, the specification discloses frizzled 2 as an exemplary frizzled protein for the development of antibodies that inhibit malignant cell growth, and contemplates other frizzled proteins (total 10 frizzled receptor proteins, [~]frizzled 5 is one member) family and can be used as antigens to develop antibodies for immunotherapy.

The above disclosure reasonably communicates that there are 10 frizzled proteins, and contemplates a genus directed to all of the 10 frizzled proteins. However, the claimed subgenus, i.e. group of either monoclonal or human antibodies directed to any one of the numerous epitope that could result from the 235-amino acid N-terminal

extracellular domain, wherein the subgenus inhibits growth of the malignant cell that expresses the frizzled 5 receptor is not contemplated in the specification as originally filed.

The rejections of the claims under 35 U.S.C. 112, first paragraph, as failing to comply with the **enablement requirement is withdrawn** in view of applicant's argument.

The Following Are New Grounds of Rejection

Claim Rejections - 35 USC § 103

Claims 1-8, 16, 28, and 29 rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka et al (IDS, #1711998, Proc. Natl. Acad. Sci. USA. vol. 95, pages 10164-9) in view of US Pat. 5,677,171 (IDS, Hudziak et al., Oct. 14, 1997).

Claims 1-8, 16, 28, and 29 are drawn to a purified antibody binds to an epitope at the N-terminal extracellular domain (SEQ ID NO: 68) or pharmaceutical comprising said antibody, wherein the antibody inhibits growth of a malignant cell expressing a frizzled 5 receptor.

Tanaka et al., teach (note page 10164, right column under the heading Cloning of the Human FZ Genes, and also page 10165, left column under the heading "Identification of Human Esophageal Carcinoma-Specific Fz Gene) that the frizzled 5 receptor protein comprising instant SEQ ID NO: 68 is isolated from a human esophageal carcinoma tissue. Note the sequence alignment provided with the Office action mailed on 08/04/2003. This clearly indicates that a malignant esophageal cell

express the human frizzled 5 protein. Tanaka et al., at the paragraph bridging pages 10164-5 teach that N-terminal extracellular domain of a frizzled receptor lies just before the first transmembrane helix, also teach "the ectodomain of Fz functions as natural antagonist of Fz-mediated signal transduction". Tanaka et al., at page 10164 teach Wnt binds to Frizzled family of seven-transmembrane proteins, and the seven-transmembrane proteins frizzled family proteins act as receptors for Wnt oncoprotein (i.e. proteins involved in tumor). This suggests frizzled member proteins in tumor development and importance of extracellular domain of frizzled receptor for receptor-mediated signal for wnt-mediated oncogenic process.

Tanaka et al., do not teach an antibody that inhibits growth of a malignant cell expressing the receptor.

However, Hudziak patent teaches at column 5, lines 16 and 17, "antibodies to inhibit the growth of tumor cells"; at column 6 lines 5-13 "Advantageously antibodies are selected which greatly inhibit the receptor function by binding the steric vicinity of the ligand binding site of the receptor (blocking the receptor), and/or which bind the growth factor in such a way as to prevent (block) the ligand from binding to the receptor. These antibodies are selected using conventional in vitro assays for selecting antibodies which neutralize receptor function." This suggests that an antibody binding to extracellular domain, where the natural ligand binds to, would inhibit the function of the receptor. Hudziak patent also teaches assays to screen an antibody that inhibits growth of the malignant cell. Hudziak patent teaches a cytotoxic response and label at claims 1-39.

Therefore one of ordinary skill would have been motivated to screen an antibody binding to the extracellular domain (i.e. the natural ligand binding site) of frizzled 5 protein, which is expressed on a malignant cell as taught by Tanaka et al., wherein the antibody inhibits the growth of the malignant cells since the screening assay is taught by Hudziak patent. It would have been obvious to one of ordinary skill in the art to make and use an antibody directed the extracellular domain of a receptor because of the advantage as taught by the Hudziak patent. Further, one of ordinary skill would be motivated to screen an antibody inhibiting cancer cells because this kind of antibody could be used in cancer treatment as taught by Hudziak patent, and cancer treating antibody would make money.

In addition, based on *Noelle v. Lederman*, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004), an antibody to known antigenic sequence is obvious, and one of skill would have been arrived at the claimed invention with a reasonable expectation of success, given the amino acid sequence has been known, the extracellular domain of a frizzled 5 is where the natural ligand binds to, had been well known in the art before the effective filing date of the instant application as taught by Tanaka et al., and also given that advantage of the antibody to extracellular domain and an assay to isolated an antibody inhibiting the growth of a malignant cell had been known in the art as taught by Hudziak patent well before the effective filing date of the instant application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-

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272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



MISOOK YU, Ph.D.
Primary Examiner
Art Unit 1642